REMARKS

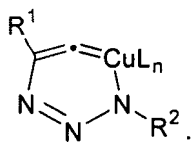
Claims 9, 26, 28, and 30 have been amended so as to correct various spelling and grammatical errors.

Rejection under 35 USC 112, first paragraph:

Claims 23 and 24 are composition claims directed to reactive intermediates produced during a metal catalyzed click chemistry cycloaddition reaction for forming triazoles. Claims 23 and 24 have been rejected under 35 USC 112, first paragraph, for allegedly failing to comply with the written description requirement. More particularly, it is alleged that the phrases "4-triazole substituent" (R^1) and "1-triazole substituent" (R^2) as employed in Claims 23 and 24 are unsupported by the specification and are not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the invention at the time the application was filed. Applicant traverses this basis for rejection.

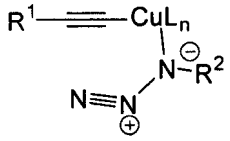
Firstly, the written description requirement with respect to the phrases "4-triazole substituent" (R^1) and "1-triazole substituent" (R^2), as employed in Claim 23, are supported in the specification as follows:

> "Another aspect of the invention is directed to a reactive intermediate for producing a product having triazole moiety. The reactive intermediate is represented by the following 6-membered ring structure:



> In the above structure, **R^1 is a 4-triazole substituent, R^2 is a 1-triazole substituent**, L is a Cu ligand, and "n" is 1, 2, or 3." (Specification, page 6, lines 15-17)

Additionally, the written description requirement with respect to the phrases "4-triazole substituent" (R^1) and "1-triazole substituent" (R^2), as employed in Claims 24, is supported in the specification as follows:

> "Another aspect of the invention is directed to a reactive intermediate for producing a triazole. The reactive intermediate is represented by the following 6-membered ring structure:
>
> 
>
>
> In the above structure, **R^1 is employable as a 4-triazole substituent, R^2 is employable as a 1-triazole substituent**, L is a Cu ligand, and "n" is 1, 2, 3, or 4." (Specification, page 6, lines 25-29.)

Secondly, the numbering employed in the phrases "4-triazole substituent" (R^1) and "1-triazole substituent" (R^2) is both conventional and supported by the specification. In a disubstituted [1,2,3] triazole having one substituted ring nitrogen, the convention is that the number "1" position of the triazole ring is the substituted ring nitrogen and that the numbering then proceeds in the direction of the ring nitrogen adjacent to the substituted ring nitrogen. This conventional numbering system is illustrated in Figure 1A and further supported in Figure 2.

Thirdly, the specification clearly conveys to persons skilled in the art that the inventors had possession of their claimed invention. More particularly, persons skilled in the art would understand that, when the specification employs the phrases "4-triazole substituent" (R^1) and "1-triazole substituent" (R^2), these phrases are employed in the context of reactive intermediates produced during metal catalyzed click chemistry cycloaddition reactions for forming triazoles and are accorded breadth consistent with that context. Persons skilled in the art would understand from the specification that the scope of these phases, when employed in the context of the present application, is broad:

> "The process is experimentally simple and appears to have enormous scope." (Specification, page 8, lines 23-24)

> "The scope of this copper-catalyzed triazole synthesis is partly revealed by the examples in Figures 3A and B; note especially the lack of functional group interference. These triazoles are obtained using a procedure which generally involves little more than stirring the reagents and filtering off pure products. Variously substituted primary, secondary, tertiary, and aromatic azides readily participate in this transformation. Tolerance for variations in the acetylene component is also excellent." (Specification: page 9, line 31 - page 10, line 5)

> "The Cu^I-catalyzed transformation described here – a high-yielding and simple to perform 'fusion' process leading to a thermally and hydrolytically stable triazole connection – is an ideal addition to the family of click reactions. The

process exhibits broad scope and provides 1,4-disubstituted [1,2,3]-triazole products in excellent yields and near perfect regioselectivity. The reactivity of copper(I) acetylides with organic azides is disclosed herein to be effectively unstoppable." (Specification: page 11, lines 6-12)

"This new catalytic process offers an unprecedented level of selectivity, reliability and scope for those organic synthesis endeavors which depend on the creation of covalent links between diverse building blocks. Several applied projects which highlight the capabilities of the process are illustrated in Figures 6-8." (Specification: page 11, lines 14 - 17)

The truly extraordinary extent of the orthogonality of the claimed click chemistry reaction is further supported and dramatically demonstrated by a disclosure that the claimed click chemistry reaction is orthogonal to both human plasma and whole human blood (Specification, page 15, lines 11-16).

Evidentiary support for the understanding of persons skilled in the art regarding the meaning of the phrases "4-triazole substituent" (R^1) and "1-triazole substituent" (R^2) in the context of Claims 23 and 24 of the present application can be found in the inventors' publication upon which the present application is based, viz., Rostovtsev, et al., *Angewandte Chemie Int. Ed., 41,* p 2596-2599 (2002). (copy in Evidentiary Appendix). Please note that Figure 1 and Scheme 1 of Rostovtsev correspond precisely to Figures 1A and 2 of the present application. Please also note that Rostovtsev describes the reactant R^1——≡ as a "terminal acetylene" and the reactant R^2——$\overset{\ominus}{N}$——$\overset{\oplus}{N}$≡N as an "azide" (Rostovtsev, page 2597, column 1, third paragraph). Rostovtsev further discloses that, after the reaction is complete, the (R^1)

substituent ends up at the 4 position of the triazole and that the (R^2) substituent ends up at the 1 position of the triazole. Persons skilled in the art, would appreciate that the (R^1) substituent of Rostovtsev's "terminal acetylene" corresponds to Applicant's "4-triazole substituent" (R^1) of the present application and that the (R^2) substituent of Rostovtsev's "azide" corresponds to Applicant's "1-triazole substituent" (R^2) of the present application.

Publication of the Rostovtsev reference by *Angewandte Chemie Int. Ed.*, is an indication that the editors of *Angewandte Chemie Int. Ed.* understood the content of Rostovtsev and understood that the authors were in possession of the content thereof. By implication, editors of *Angewandte Chemie Int. Ed.* would have also understood that the specification of the present application discloses that the inventors were in possession of their invention at the time that the present application was filed, including possession of the meaning of the phrases "4-triazole substituent" (R^1) and "1-triazole substituent" (R^2) as employed in Claims 23 and 24.

Laudatory references (see Evidentiary Appendix) cite Rostovtsev and comment on its disclosure. These comments within the laudatory references support a finding that persons skilled in the art understood that Rostovtsev was in possession of his disclosure and, by implication, the inventors of the present application were in possession of their invention. More particularly, the laudatory references support a finding that the (R^1) substituent of Rostovtsev's "terminal acetylene" and the (R^2) substituent of Rostovtsev's "azide" were employable in a click chemistry reaction for forming a disubstituted triazole, wherein the 1-position of the triazole has the (R^2) substituent and the 4-position of the triazole has the (R^1) substituent. By implication, these laudatory references also support a finding that persons skilled in the art would have understood that the inventors of the present application were in possession of their invention and that, more particularly, the metes and bounds of the phrases "4-

triazole substituent" (R^1) and "1-triazole substituent" (R^2), as employed in Claims 23 and 24, would have been understood and that these phrases are fully supported by the specification.

Withdrawal of the rejection of claims 23 and 24 for failure to comply with the written description requirement is respectfully requested.

Rejection under 35 USC 112, second paragraph:

Claims 1-30 are rejected under 35 USC 112, second paragraph on the basis that the claims are indefinite. More particularly, the following words and phrases (items 1-10) are alleged to be indefinite:

1. "a first reactant having a terminal alkyne moiety";
2. "a second reactant having an azide moiety";
3. "a product having a triazole moiety";
4. "a triazole";
5. "a polyvalent triazole";
6. "a polyazide core";
7. "a molecule having a terminal alkyne";
8. "a product containing a [1,2,3]-triazole";
9. "a first reactant having a monosubstituted alkyne";
10. "a reactant having an azide".

The Examiner suggests that this basis for rejection may be overcome by inserting the corresponding formulas into the claims. Applicant traverses this basis for rejection.

The CAFC has defined the test for definiteness:

> "The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 [second paragraph] demands no more. The degree of precision necessary for adequate claims is a function of the nature of the subject matter." *(Miles Lab., Inc., v Shandon, Inc.* 997 F.2nd 870, 875, 27 U.S.P.Q.2D 1123, 1126 (Fed. Cir. 1993) (internal citations omitted)

Further factors determinative of the definiteness standard were provided by the CCPA:

> "[T]he definiteness of the language employed must be analyzed - not in a vacuum, but always in light of the teaching of the prior art and the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore*, 169 U.S.P.Q. 236, 238 (CCPA 1971)

A major aspect of the present invention is directed to a process for the metal catalysis of click chemistry cycloaddition reactions between azides and terminal acetylenes for producing disubstituted [1,2,3,] triazoles. The cycloaddition of azides and alkynes to give triazoles was known in the prior art. (R. Huisgen, *Pure Appl. Chem.* **1989**, *61*, 613-628; R. Huisgen, et al., *Chem. Ber.* **1967**, *100*, 2494-2507; W. Lwowski, in *1,3-Dipolar Cycloaddition Chemistry*, (Ed.: A. Padwa), Wiley, New York, **1984**; Vol. 1, Chapter 5; and J. Bastide, et al., *Bull. Soc. Chim. Fr.* **1973**, 2555-2579; 2871-2887).

Indeed, a click chemistry version of this cycloaddition reaction had been known (W. G. Lewis, et al., *Angew. Chem. Int. Ed.* **2002**, *41*, 1053-1057). What was not known in the prior art was metal catalysis for this cycloaddition reaction and the enhanced properties brought about by the use of metal catalysis.

Miles Lab case states that "the degree of precision necessary for adequate claims is a function of the nature of the subject matter." *In re Moore* states that definiteness must be analyzed in light of the teachings of the prior art. In effect, when a claim element is taught in the prior art, the definiteness of such element must be sufficient, when assessed in light of both the specification and the prior art, to reasonably apprise those skilled in the art of the scope of such element.

The specification discloses that the processes covered by Claims 1-22 and 27-30 are generic and are not limited to specific formulae.

> "The process is experimentally simple and appears to have enormous scope." (Specification, page 8, lines 23-24)

The phrases "a first reactant having a terminal alkyne moiety," "a second reactant having an azide moiety," "a molecule having a terminal alkyne," "a product containing a [1,2,3]-triazole," "a first reactant having a monosubstituted alkyne," and "a reactant having an azide," are generic expressions for claim elements that were known, at least in part, in the prior art. When interpreted within the context of a metal catalyzed click chemistry reaction as disclosed in light of the specification and within the context of related prior art, each of the above phrases has sufficient particularity to reasonably apprise persons skilled in the art of the scope of the elements they represent and of the claims in which they appear, viz. claims 1-22 and 27-30. The above phrases satisfy the criteria for definiteness under the rule of *Miles Lab.*. Applicant is not required under the

Miles Lab standard to replace these phrases with formulae.

Claim 23 is composition claim that employs the phrase "product having a triazole moiety". The composition of Claim 23 is novel. However, its structure is depicted with sufficient particularity in such claim to reasonably apprise a person skilled in the art of the scope of the claim. The phrase "product having a triazole moiety" satisfies the criteria for definiteness under the rule of *Miles Lab.*.

Claim 24 is composition claim and Claim 25 is a process claim having two steps that employ the a word "triazole" for describing the product. In Claim 24, this product is novel. However, its structure is depicted with sufficient particularity to apprise a person skilled in the art of the scope of the claim. In Claim 24, the product includes species that were known in the prior art and is reasonably sufficient in particularity to reasonably apprise persons skilled in the art of the scope of the claim and to satisfy the criteria for definiteness under the rule of *Miles Lab.*.

Claims 26 and 27 are process claims for producing "polyvalent triazoles". Support for making "polyvalent triazoles" using various "polyazide cores" is found in Figure 7 and in the Specification at page 7, lines 6-9 and at page 8, lines 15-16. Support for making "polyvalent triazoles" using various "polyalkyne cores" is found in Figure 8 and in the Specification at page 7, lines 11-14 and at page 8, lines 18-19.

The phrase "polyazide core" would be understood by a person skilled in the art, in view of the specification of the present application, to mean any reactant employable in the reaction of Claim 26 having two or more azide moieties. The phrase "polyazide core" satisfies the criteria for definiteness under the rule of *Miles Lab., Inc., v Shandon, Inc.* Applicant cannot be required to replace this phrase with a formula.

The phrase "polyvalent triazole" would be understood by a person skilled in the art, in view of the specification of the present application, to mean any product of the reaction of either Claim 26 or 27, wherein the product has two or more newly formed triazoles. The phrase "polyvalent triazole" satisfies the criteria for definiteness under the rule of *Miles Lab.*. Applicant cannot be required to replace this phrase with a formula.

Summary:

Claims 1-30 are pending. Claims 9, 26, 28, and 30 have been amended so as to correct various spelling and grammatical errors. Claims 23 and 24 have been rejected as failing to be supported by the written description requirements; Claims 1-30 have been rejected as indefinite. Withdrawal of both of these bases for rejections is requested in view of the arguments, cited case law, and evidence, in the form of laudatory references. Allowance of all claims, i.e., claims 1-30, is respectfully requested.

Respectfully submitted,

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